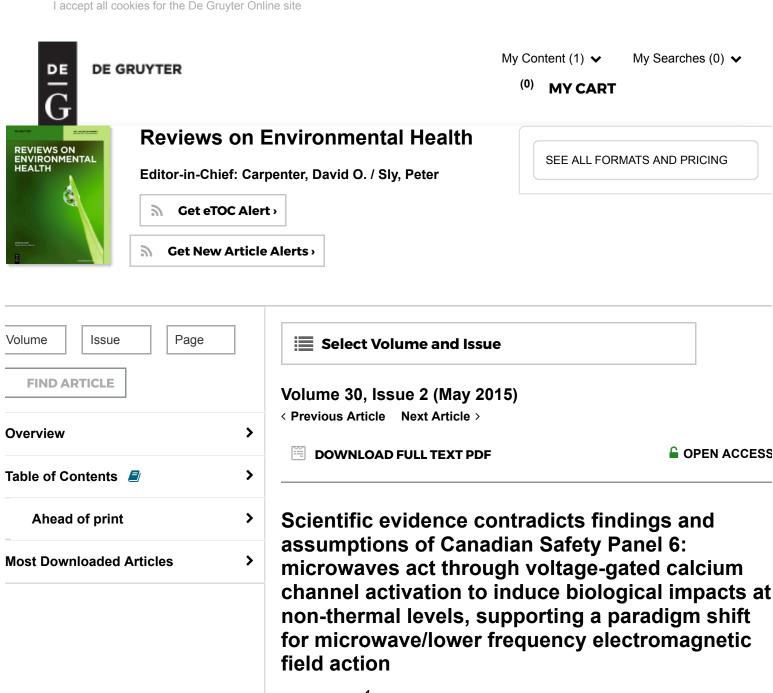
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Abstract

This review considers a paradigm shift on microwave electromagnetic field (EMF) action from only thermal effects to action via voltage-gated calcium channel (VGCC) activation. Microwave/lower frequency EMFs were shown in two dozen studies to act via VGCC activation because all effects studied were blocked by calcium channel blockers. This mode of action was further supported by hundreds of studies showing microwave changes in calcium fluxes and intracellular calcium [Ca2+]i signaling. The biophysical properties of VGCCs/similar channels make them particularly sensitive to low intensity, non-thermal EMF exposures. Nonthermal studies have shown that in most cases pulsed fields are more active than are non-pulsed fields and that exposures within certain intensity windows have much large biological effects than do either lower or higher intensity exposures; these are both consistent with a VGCC role but inconsistent with only a heating/thermal role. Downstream effects of VGCC activation include calcium signaling, elevated nitric oxide (NO), NO signaling, peroxynitrite, free radical formation, and oxidative stress. Downstream effects explain repeatedly reported biological responses to non-thermal exposures: oxidative stress; single and double strand breaks in cellular DNA; cancer; male and female infertility; lowered melatonin/sleep disruption; cardiac changes including tachycardia, arrhythmia, and sudden cardiac death; diverse neuropsychiatric effects including depression; and therapeutic effects. Non-VGCC non-thermal mechanisms may occur, but none have been shown to have effects in mammals. Biologically relevant safety standards can be developed through studies of cell lines/cell cultures with high levels of different VGCCs, measuring their responses to different EMF exposures. The 2014 Canadian Report by a panel of experts only recognizes thermal effects regarding safety standards for non-ionizing radiation exposures. Its position is therefore contradicted by each of the observations above. The Report is assessed here in several ways including through Karl Popper's assessment of strength of evidence. Popper argues that the strongest type of evidence is evidence that falsifies a theory; second strongest is a test of "risky prediction"; the weakest confirms a prediction that the theory could be correct but in no way rules out alternative theories. All of the evidence supporting the Report's conclusion that only thermal effects need be considered are of the weakest type, confirming prediction but not ruling out alternatives. In contrast, there are thousands of studies apparently falsifying their position. The Report argues that there are no biophysically viable mechanisms for non-thermal effects (shown to be false, see above). It claims that there are many "inconsistencies" in the literature causing them to throw out large numbers of studies; however, the one area where it apparently documents this claim, that of genotoxicity, shows no inconsistencies; rather it shows that various cell types, fields and end points produce different responses, as should be expected. The Report claims that cataract formation is produced by thermal effects but ignores studies falsifying this claim and also studies showing [Ca2+]i and VGCC roles. It is time for a paradigm shift away from only thermal effects toward VGCC activation and consequent downstream effects.

Keywords: <u>calcium and nitric oxide signaling</u>; <u>calcium channel blockers</u>; <u>low level microwave/radiofrequency radiation</u>; <u>oxidative and nitrosative stress</u>; <u>peroxynitrite</u>

☐ Introduction

There has been a literature reporting various non-thermal effects of microwave/radiofrequency radiation exposures starting with the Soviet literature in the 1950s. Subsequently, there have been thousands of international published studies reporting non-thermal or what are sometimes called microthermal effects producing therapeutic responses, changes in calcium fluxes and signaling, increased oxidative stress, and a wide variety other health-related responses in humans and animal models.

Nevertheless, there has been a series of medical reports, arguing that only thermal effects need be considered when setting guidelines or safety standards for microwave electromagnetic field (EMF) exposures. These have been based mainly on two types of arguments:

- That there cannot be any biophysically viable mechanism for any such nonthermal effects and therefore that reports of such effects should be viewed with great skepticism.
- 2. That there are many "conflicts" or "inconsistencies" in the literature which according to these reports, justify rejection of the various thousands of publications showing apparent non-thermal effects.

The focus of this review is to consider whether it is time for a "paradigm shift" away from strictly thermal effects toward non-thermal effects. Specifically, it is focused on the recent finding that most, possibly all non-thermal effects can be produced by microwave activation of voltage-gated calcium channels (VGCCs).

It is also focused on the 2014 Report of the Canadian Panel of Experts on Safety Code 6 as the most recent and therefore up-to-date summary of the evidence supporting the strictly thermal point of view.

- (VGCCs) assumptions of current safety standards channels may make them uniquely susceptible to low intensity MF activation radiofrequency fields **⊞** What is in the report? **⊞** Genotoxicity of non-thermal microwave exposures: examples of inconsistency? Harl popper and how to assess scientific evidence **B** Some other aspects heating **⊞** Summary of the report **⊞** How VGCC activation by microwave/RF exposure can produce a variety of important biological responses **⊞** Biologically-based EMF safety standards **⊞** Brief overview **Acknowledgments** □ References
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